

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-3, 5-8, 10-13, 15-18, 20-26, 28-31, 33-36 and 44-59 are pending in the application, with claims 1, 8, 24, 31 and 44 being the independent claims. Claims 1, 8, 24, 31 and 47 are sought to be amended. These changes are believed to introduce no new matter, and their entry is respectfully requested.

As noted below, the present Office Action was improperly made final. Therefore, the amendments set forth herein should be entered and considered. Should the finality of the Office Action not be withdrawn, Applicants note that the amendments set forth herein present the claims in better form for consideration on appeal and therefore should be entered in accordance with 37 C.F.R. § 1.116(b).

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Improper Final Office Action

The present Office Action was improperly made final. According to the MPEP § 706.07(a), a second or subsequent action on the merits should not be made final if the Examiner introduces a new ground of rejection that is neither necessitated by an Applicant's amendment of the claims nor based upon information submitted in an information disclosure statement filed during the period set forth in 37 C.F.R. § 1.97(c). Here the Examiner has

introduced new grounds of rejection that were not necessitated by Applicants' claim amendments, and were not based upon information submitted in an information disclosure statement filed during the period set forth in 37 C.F.R. § 1.97(c). Therefore the Office Action should not have been made final.

The Examiner stated that Applicants' amendment necessitated the new grounds of rejection. *See* Office Action dated October 9, 2003, page 5. As explained below, the new grounds of rejection could have been applied to the claims as presented *prior* to Applicants' Amendment and Reply filed on August 5, 2003 ("the August 5, 2003 Amendment"). Thus, the amendments did not necessitate the new grounds of rejection.

The Examiner made two rejections under 35 U.S.C. § 112, second paragraph, that were not necessitated by the amendments. The rejections were based on the recitation of 3-hydroxy-2-pyridinemaltol and 3-hydroxy-2-pyridineethyl maltol, in claims 1 and 24, respectively. *See* Office Action dated October 9, 2003, page 2. Although these terms were not found in claims 1 and 24 prior to the August 5, 2003 Amendment, they were found in claims 4 and 27 prior to the amendment. *See* claims 4 and 27 as originally presented. Claims 1 and 24 were amended to incorporate the language of claims 4 and 27 into claims 1 and 24, respectfully. The rejections under 35 U.S.C. § 112, second paragraph, could have been applied to claims 4 and 27. The changes made to claims 1 and 24 in the August 5, 2003 Amendment therefore did not necessitate the new grounds of rejection under 35 U.S.C. § 112, second paragraph.

The Examiner also made rejections under 35 U.S.C. § 102 that were not necessitated by the August 5, 2003 Amendment. In particular, claims 8 and 31 were rejected as being anticipated by Chenoufi or Ward, claims 24-26, 31, 34 and 35 were rejected as being

anticipated by Gaut, and claims 31 and 33 were rejected as being anticipated by Murad. *See* Office Action dated October 9, 2003, pages 3-4. These rejections could have been applied to the claims pending in the application before the August 5, 2003 Amendment.

Claims 8 and 31, as they existed prior to the August 5, 2003 Amendment, encompassed the subject matter defined by claims 8 and 31 *after* the August 5, 2003 Amendment. Any subject matter allegedly falling within the scope of claims 8 and 31 after the August 5, 2003 Amendment necessarily would have fallen within the scope of claims 8 and 31 prior to the amendment. It therefore follows that any anticipation rejections that are applied to amended claims 8 and 31 could have been applied to claims 8 and 31 prior to the August 5, 2003 Amendment.

In addition, the scope of claim 8, as presented in the August 5, 2003 Amendment, is identical to the scope of dependent claim 9, which was pending in the application prior to the August 5, 2003 Amendment, except for the deletion of pyridoxal isonicotinyl hydrazone in amended claim 8. Likewise, the scope of claim 31, as presented in the August 5, 2003 Amendment, is identical to the scope of dependent claim 32, which was pending in the application prior to the August 5, 2003 Amendment, except for the deletion of pyridoxal isonicotinyl hydrazone in amended claim 31. The new § 102 rejections of claims 8 and 31 could have been applied to claims 9 and 32 before the August 5, 2003 Amendment. The amendments to claims 8 and 31 therefore did not necessitate the new grounds of rejection under 35 U.S.C. § 102.

In summary, the new grounds of rejection under 35 U.S.C. §§ 112 and 102 could have been applied to the claims that were pending in the application prior to the August 5, 2003 Amendment. Thus, the claim amendments did not necessitate the new grounds of rejection.

Accordingly, the present Office Action should not have been made final. Applicants respectfully request that the finality of the Office Action be reconsidered and withdrawn.

II. Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-3, 8, 11, 12, 15-18, 20-24, 31, 54 and 55 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. *See* Office Action dated October 9, 2003, page 2. This rejection is based on the recitation of "3-hydroxy-2-pyridinemaltol" in claim 1 and "3-hydroxy-2-pyridineethyl maltol" in claim 24. According to the Examiner, these are not known compounds. Applicants respectfully traverse this rejection. Nonetheless, solely to expedite prosecution, Applicants have deleted "3-hydroxy-2-pyridinemaltol" from claim 1 and "3-hydroxy-2-pyridineethyl maltol" from claim 24. Thus, this ground of rejection is fully accommodated and should be withdrawn.

The Examiner also pointed out that 3-hydroxypyrid-2-one is the same as 3-hydroxy-2(1H)-pyridinone¹, and that both terms are recited in claims 8 and 31. *See* Office Action dated October 9, 2003, page 3. Applicants have deleted "3-hydroxy-2(1H)-pyridinone" from claims 8 and 31. This basis of rejection is therefore fully accommodated and should be withdrawn.

Finally, the Examiner noted that nicotinic acid-N-oxide is "misclassified" as a hydroxypyridine derivative in claims 8 and 31. *See* Office Action dated October 9, 2003, page 3. Applicants have deleted "nicotinic acid-N-oxide" from claims 8 and 31. This basis

¹The Examiner used the term "3-hydroxy-2(1H)-pyridone" in the Office Action. Applicants believe that the Examiner intended to use the term "3-hydroxy-2(1H)-pyridinone," since this is the term used in the CA Registry print-out that was attached to the Office Action as document [U] and was recited in claims 8 and 31.

of rejection is therefore fully accommodated and should be withdrawn.

III. Claim Rejections Under 35 U.S.C. § 102

A. Chenoufi or Ward

Claims 8 and 31 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Chenoufi *et al.*, *J. Hepatol.* 23:166-173 (1995) ("Chenoufi") or Ward and Harris, *Aust. J. Biol. Sci.* 29:189-196 (1976) ("Ward"). *See* Office Action dated October 9, 2003, page 3. Applicants respectfully traverse this rejection.

Chenoufi refers to 1,2-dimethyl-3-hydroxypyridin-4-one (CP20), which is added to a culture medium. Ward refers to Waymouth's medium containing, *inter alia*, 3-hydroxy-4-(1H)-pyridone. Applicants note that 1,2-dimethyl-3-hydroxypyrid-4-one and 3-hydroxypyrid-4-one are not included among the transition metal-binding compounds recited in claims 8 and 31 as currently presented. Neither Chenoufi nor Ward teach a serum-free cell culture medium that falls within the scope of claims 8 or 31. Thus, neither Chenoufi nor Ward anticipate the present claims. Applicants respectfully request that this rejection be reconsidered and withdrawn.

B. Gaut

Claims 24-26, 31, 34 and 35 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Gaut and Solomon, *Biochim. Biophys. Acta* 201:316-322 (1970) ("Gaut"). *See* Office Action dated October 9, 2003, page 3. Applicants respectfully traverse this rejection.

Claims 24 and 31 are directed to serum-free cell culture media capable of supporting the cultivation of a cell *in vitro*. Gaut refers to experiments in which radiolabeled nicotinic acid and various nicotinic acid analogs were added to human platelets in Ca^{2+} - and Mg^{2+} -free Krebs-Ringer bicarbonate buffer. *See* Gaut at page 317, first full paragraph. The buffer used in Gaut is not a serum-free cell culture medium capable of supporting the cultivation of a cell *in vitro*. Gaut therefore does not teach all of the elements of claims 24 or 31 or the claims that depend therefrom. Thus, Gaut does not anticipate claims 24-26, 31, 34 and 35. Applicants respectfully request that this rejection be reconsidered and withdrawn.

C. Murad

Claims 31 and 33 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,328,913 to Murad *et al.* ("Murad"). *See* Office Action dated October 9, 2003, page 4. Applicants respectfully traverse this rejection.

Claim 31, as currently presented, is directed to serum-free cell culture media capable of supporting the cultivation of a cell *in vitro*. The medium of Murad includes calf serum, *i.e.*, it is not a serum-free medium. *See* Murad at column 5, lines 17-24 and 26-29. Murad therefore does not teach all of the elements of claim 31 or the claims that depend therefrom. Thus, Murad does not anticipate claims 31 and 33. Applicants respectfully request that this rejection be reconsidered and withdrawn.

IV. Claim Rejections Under 35 U.S.C. § 103

Claims 44-47 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Landschulz *et al.*, *J. Cell Biol.* 98:596-601 (1984) ("Landschulz") or Murad. *See* Office

Action dated October 9, 2003, pages 4-5. Applicants respectfully traverse this rejection.

Claim 44 is directed to a kit for the cultivation of a cell *in vitro*, said kit comprising:

- (a) at least one first container containing at least one first component selected from the group consisting of one or more cell culture media or media ingredients, and one or more cells, and
- (b) at least one second container containing at least one second component selected from the group consisting of one or more transition metal binding compounds and at least one transition element complex, said complex comprising at least one transition element or a salt or ion thereof complexed to at least one transition metal-binding compound.

In order to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. *See In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). The teaching or suggestion to make the claimed combination must both be found in the prior art, not in Applicants' disclosure. *See In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Importantly, evidence of a suggestion or motivation to combine references must be "clear and particular." *See In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999). "Broad conclusory statements regarding the teaching of multiple references, standing alone, are not 'evidence.'" *Dembiczak*, 175 F.3d at 999, 50 USPQ2d at 1617. Here, a *prima facie* case of obviousness has not been established because a person of ordinary skill in the art would not have been motivated to modify Landschulz or Murad to produce a kit that falls within the scope of the present claims.

In support of the obviousness rejection, the Examiner pointed to Figure 3 of Landschulz. According to the Examiner,

the first point of the curve of Figure 3, shows cells + medium which is component A of the claimed composition and the other points on the curve show cells + medium + isonicotinoyl hydrazone, component B of the claimed composition.

See Office Action dated October 9, 2003, page 5. The Examiner's reasoning appears to be that a person of ordinary skill in the art, based solely on Figure 3 of Landschulz, would have been motivated to produce a kit comprising individual containers, wherein the individual containers contain the reagents that were used to generate the individual data points of Figure 3. Applicants respectfully submit that there is nothing in Landschulz that would have suggested producing such a kit.

The Experiments in Landschulz were conducted in order to determine the effect of various concentrations of ferric pyridoxal isonicotinoyl hydrazone (FePIH) on thymidine incorporation and DNA content of tissues. It appears from Landschulz that, in generating the data for Figure 3, multiple cultures were used, each containing different amounts of FePIH, including one that contained no FePIH. Landschulz does not suggest, however, that the individual cultures used to generate the data points in Figure 3 should have been saved and collected together to produce a kit. A person of ordinary skill in the art would have expected that, once the individual data points were obtained, the cultures -- which contained radioactive thymidine -- would have been discarded as soon as possible and not collected to form a kit. The Examiner has not pointed to anything specific in Landschulz suggesting that the cultures used to produce the individual data points of Figure 3 should have been collected into a kit for any purpose. A *prima facie* case of obviousness cannot be established based solely on Figure 3 of Landschulz.

The Examiner also asserted that:

mere separation or division of a known composition of US

5,328,913 [Murad] or Landschultz [sic: Landschulz] *et al.* into components which are meant to be combined prior to usage is obvious in the absence of unexpected result due to separation of the components.

See Office Action dated October 9, 2003, page 5. Applicants respectfully submit that this assertion cannot support a *prima facie* case of obviousness. First, this assertion is not supported by any "clear and particular" evidence, as required by the Federal Circuit. See *Dembiczak*, 175 F.3d at 999, 50 USPQ2d at 1617. The Examiner has not pointed to anything which supports the conclusion that dividing the various components recited in Murad or Landschulz into a kit would have been obvious. Second, the Examiner is reminded that the Examiner has the initial burden of establishing a *prima facie* case of obviousness. According to the MPEP § 2142, "[t]he examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness." Thus, the Examiner cannot establish a *prima facie* case of obviousness simply by asserting that Applicants have not demonstrated unexpected results.

In summary, the Examiner has not put forth any valid evidence to support the conclusion that, based on Landschulz or Murad, it would have been obvious to produce the kits encompassed by claims 44-47. Thus, a *prima facie* case of obviousness has not been established. Applicants therefore respectfully request that the rejection under 35 U.S.C. § 103 be reconsidered and withdrawn.

V. Claim Objections

Claim 10 was objected to as being dependent upon a rejected base claim. See Office Action dated October 9, 2003, page 5. As noted above, Applicants believe that the rejections

of claim 8, from which claim 10 depends, have been fully accommodated by the amendments set forth herein. Therefore, Applicants respectfully request that the objection to claim 10 be reconsidered and withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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